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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,500	03/24/2004	Eberhard Weihe	029310.53352US	4381

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EXAMINER	
ULM, JOHN D	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/29/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/807,500	WEIHE ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8-20,25,26,28-33,35-39,44,45,47,49,54,55 and 57-65* is/are pending in the application.

4a) Of the above claim(s) *18-20,25,26,28-33,35-39,44,45,47 and 63-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8-17,49,54,55 and 57-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/09/04,12/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1) Claims 1 to 5, 8 to 20, 25, 26, 28 to 33, 35 to 39, 44, 45, 47, 49, 54, 55 and 57 to 65 are pending in the instant application. Claims 1, 13, 14, 20, 28 to 30, 33, 35 to 37, 39, 44, 45, 47, 49, 54, 55 and 57 have been amended, and claims 6, 7, 21 to 24, 27, 34, 40 to 43, 46, 48, 50 to 53 and 56 have been canceled as requested by Applicant in the correspondence filed 20 July of 2006.

2) Claims 18 to 20, 25, 26, 28 to 33, 35 to 39, 44, 45, 47 and 63 to 65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 20 July of 2006. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3) The amendment to the claims that was filed on 20 July of 2006, and particularly pages 23 and 24 therein, does not comply with 37 C.F.R. 1.52 (b) with respect to line spacing. 37 C.F.R. 1.52 (b) states that:

> " Except for drawings, the **application papers** (specification, **including claims**, abstract, oath or declaration, and papers as provided for in this part) **and also papers subsequently filed**, must have each page plainly written on only one side of a sheet of paper, with the claim or claims commencing on a separate sheet and the abstract commencing on a separate sheet. See §§ 1.72(b) and 1.75(h). The sheets of paper must be the same size and either 21.0 cm. by 29.7 cm. (DIN size A4) or 21.6 cm. by 27.9 cm. (8 ½ by 11 inches). Each sheet must include a top margin of at least 2.0 cm. (3/4 inch), a left side margin of at least 2.5 cm. (1 inch), a right side margin of at least 2.0 cm. (3/4 inch), and a bottom margin of at least 2.0 cm. (3/4 inch), and no holes should be made in the sheets as submitted. The lines of the specification, and **any amendments to the specification, must be 1 ½ or double spaced**. The pages of the specification including claims and abstract must be numbered consecutively, starting with 1, the numbers being centrally located above or preferably, below, the text. See § 1.84 for drawings.

Applicant is advised that the claims are part of the specification. In responding to this office action, Applicant must supply a complete copy of the pending claims, whether amended or not, which complies with 37 C.F.R. 1.52 (b) as well as 37 C.F.R.1.121(c).

4) The instant specification does not comply with 37 C.F.R. § 1.84(U)(1), which states that partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a **capital letter**. Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(U)(1), Applicant is required to file an amendment to change the Brief Description of the Drawings and the rest of the specification accordingly.

5) The instant specification does not comply with 37 C.F.R. ∋ 1.77, which requires that:

(a) The elements of the application, if applicable, should appear in the following order:

(1) Utility Application Transmittal Form.

(2) Fee Transmittal Form.

(3) Title of the invention; or an introductory portion stating the name, citizenship, and residence of the applicant, and the title of the invention.

(4) Cross-reference to related applications.

(5) Statement regarding federally sponsored research or development.

(6) Reference to a AMicrofiche appendix.≅ (See ∋ 1.96 (c)). The total number of microfiche and total number of frames should be specified.

(7) Background of the invention.

(8) Brief summary of the invention.

(9) **Brief description of the several views of the drawing.**

(10) Detailed description of the invention.

(11) Claim or claims.

(12) Abstract of the Disclosure.

(13) Drawings.

(14) Executed oath or declaration.

(15) Sequence Listing (See ээ 1.821 through 1.825).

(b) The elements set forth in paragraphs (a)(3) through (a)(5), (a)(7) through (a)(12) and (a)(15) of this section **should appear in upper case, without underlining or bold type, as section headings**. If no text follows the section heading, the phrase ANot Applicable≅ should follow the section heading. [43 FR 20464, May 11, 1978; 46 FR 2612, Jan. 12, 1981; paras. (h) and (i), 48 FR 2712, Jan. 20, 1983, effective Feb. 27, 1983; revised, 61 FR 42790, Aug. 19, 1996, effective Sept. 23, 1996].

Correction is required.

6) The drawings in the instant application do not comply with 37 C.F.R. § 1.821(d), which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. M.P.E.P. 2422.02 expressly states that "when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings". Figures 1A to 1D, for example, make reference to two specific amino acid sequences and two specific nucleotide sequences without employing the required sequence identifiers.

Correction is required.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7) Claims 1 to 5, 8 to17, 49, 54, 55 and 57 to 62 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible specific and substantial asserted utility or a well established utility. The instant claims are drawn to a method of identifying a substance as effective for the treatment of any one of a plurality of causally and mechanistically unrelated neurological disorders, and specifically visual disturbances, by identifying a compound that binds to and effects the activity of a "BNPI" protein comprising the amino acid sequence presented in SEQ ID NO:2 of the instant application. The claimed method lacks utility in currently available form for several reasons.

First, it is well established in the art of molecular biology that a compound that binds to and stimulates the activity of a particular protein is, by definition, an agonist of that protein. It is also well established in the art that a compound that binds to and suppresses the activity of a protein is defined as an antagonist of that protein. It is further well established that an agonist and an antagonist of a particular protein have opposite physiological effects when administered to an organism with respect to those physiological processes that are mediated by that particular protein. The instant claims are inoperable because they do not distinguish between an agonistic and an antagonistic compound and because the instant specification and prior art of record fail to disclose whether it is the BNPI agonist or the BNPI antagonist that provides the required beneficial effect when administered to a subject suffering from one or more of the plurality of causally and mechanistically unrelated neurological disorders, and specifically visual disturbances, that are recited in the instant claims. It is a matter of

law that an invention must have a specific and substantial utility "in currently available form", which precludes the need for further research, if that research is needed to establish a utility for the claimed invention (*Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966)). Because the instant specification leaves it to the artisan to engage in the additional experimentation needed to determine if it is the BNPI agonist or the BNPI antagonist that provides the required beneficial effect in the treatment of a particular disease, the claimed method lacks a specific and substantial utility in currently available form.

Second, there is absolutely no evidence or sound scientific reasoning of record that supports a conclusion that a compound that binds to and effects the activity of a "BNPI" protein comprising the amino acid sequence presented in SEQ ID NO:2 of the instant application will have any predictable effect whatever on any one or more of the diseases and disorders recited in the instant claims. There is no evidence that a protein of the instant invention has increased or decreased activity in any particular disease or disorder or that the stimulation or inhibition of that activity will provide therapeutically beneficial effect. Applicant is advised that a statement of a specific utility is treated as true if it would be believed to be true by one of ordinary skill in the art given the evidence of record. Because there is absolutely no evidence provided by the instant specification or the prior art of record that a transporter protein of the instant invention is involved in any specific way with any one of the plurality of causally and mechanistically unrelated neurological disorders, and specifically visual disturbances, the utilities asserted in paragraph 0022 of the instant specification are not credible to one of

ordinary skill in the art of receptor biology in view of the evidence of record, or more precisely, the lack thereof. "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record (e.g., test data, affidavits or declarations from experts in the art, patents or printed publications) that is probative of the applicant 's assertions", (M.P.E.P. 2106.02 II(b)(1)(ii)).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8) Claims 1 to 5, 8 to 17, 49, 54, 55 and 57 to 62 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Further, these claims encompass a binding assay that can employ a "BNPI" protein having other than its entire native amino acid sequence. With respect to the limitation "the protein BNPI", the metes and bounds of that limitation are undeterminable. The limitations recited in claim 1 require a protein having as few as ten consecutive amino acids from one of the four native amino acid sequence described in the instant specification, each of which is 560 amino acids in length However, the instant specification does not provide the guidance needed to practice the claimed process with a "BNPI" polypeptide comprising anything less than the entire amino acid sequence presented in SEQ ID NO:2, 4, 6 or 8. The only manner described in the

instant specification of using the claimed method is in the identification of compounds that have potential medicinal use because of their ability to agonize or antagonize one of the four mammalian transporter proteins described therein. The claimed invention is only useful in so far as the transporter protein employed in the claimed assay responds in a manner that is predictive of an authentic physiological response. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

One of ordinary skill in the art of receptor biology would not reasonably believe that the majority of physical peptide embodiments having at least to amino acids in common with SEQ ID NO:2, 4, 6 or 8 are going to be functional, much less be capable of producing an authentic response. Because the instant specification does not identify those amino acid residues in SEQ ID NO:2, 4, 6 or 8 which are critical to the structural and functional integrity of a transporter receptor protein comprising that sequence, identify a structurally analogous protein for which this information is known and could be

applied to the instant protein by extrapolation, or even provide a single working example of an intentionally modified transporter protein of the instant invention, an artisan can not change even a single residue within the amino acid sequence of SEQ ID NO:2, 4, 6 or 8 and predict the effects of that change on the performance of that protein "by resort to known scientific law". Unless one can predict, with reasonable confidence, that an intentionally modified transporter protein is going to produce a response that is predictive of a native mammalian transporter protein, the information obtained from a process that uses that modified protein is of no practical value even if that protein had an established relationship with a particular disease or disorder.

9) Claims 4, 5, 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description and enablement requirements. These claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention. These claims require the manipulation of a cell by genetic engineering to allow the measurement of at least one functional parameter modified by the binding of a test substance to a BNPI protein of the instant invention. Claim 5 requires that addition of a G protein or a reporter gene. Claims 11 and 12 require the measurement of a variety of physiological parameters other than phosphate uptake by a host cell.

However, the only measurable activity that has been demonstrated for a BNPI protein of the instant invention in either the instant specification or the art of record is the uptake of radioactive phosphate (P^{32}). No other means of measuring the activity of a BNPI protein is disclosed in the specification or the prior art of record. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one can not following the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10) Claims 1 to 5, 8 to 17, 49, 54, 55 and 57 to 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10.1) Claims 1 to 5, 8 to 17, 49, 54, 55 and 57 to 62 are vague and indefinite in so far as they employ the term "BNPI" as a limitation. Because the instant specification does not define this term nor does it identify that property or combination of properties which is unique to and, therefore, definitive of "the protein BNPI" an artisan can not determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation. Whereas prior art references such as the Ni et al. patent (5,618,677) employ the term "hBNPI protein" to described a specific Na^+ -dependent inorganic phosphate cotransporter that occurs naturally in the human brain, Applicant can not rely upon such references to define the metes and bounds of the limitations contained in the instant claims.

10.2) Claims 1 to 5 and 8 to 17 are vague and indefinite because there is no antecedent basis for "the protein BNPI". The text in paragraph 0022 of the instant specification indicates that there are at least four distinct proteins that are encompassed by the term "BNPI" as this term is employed therein.

10.3) The phrase "cultivated under conditions which allow expression" in claim 8 renders this claim vague and indefinite because the identity of the element or elements being expressed is not specified. Claim 9 is vague and indefinite in so far as it depends from claim 8 for this element.

10.4) Claim 49 is vague and indefinite because it is clearly incomplete. The text "encephalitis, demyelinisation, retinal degeneration, glaucoma, nystagmus, BNPI or a protein comprising SEQ ID NO: 2, 4, 6, or 8, or a protein which is at least 90%

homologous thereto," makes no sense. Further, there is no antecedent basis for "the biomolecule of group I" or "such a protein or partial protein". Claims 54, 55 and 57 to 62 are vague and indefinite in so far as they depend from claim 49.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11) Claims 1, 3, 8 to 10 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by the Ni et al. patent (5,618,677). The text from line 55 in column 28 to line 15 in column 29 of Ni et al. described a process of identifying "agents which act as antagonists or agonists of the hBNPI protein" by employing a "method comprising contacting a functional compound of the hBNPI protein with said substance, monitoring binding activity by physically detectable means, and identifying those substances which effect a chosen response". The method of Ni et al. is not materially different from those of the instant claims. The preamble recited in the instant claims is nothing more than a statement of intended use of a known process and does not materially distinguish the claimed process from the prior art since both process achieve the same objective of identifying compounds that effect the activity of a BNPI protein. See M.P.E.P. 2111.02(II).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JOHN ULM
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GROUP 1649